AUG 2 0 2001

Summary of Safety and Effectiveness

As required by 21 CFR 807.92, the following 510(k) Summary is provided:

1. **Submitters Information**

Contact person: William J. Pignato
Director of Regulatory Affairs

Address: Bayer Diagnostics Corporation
63 North Street
Medfield, MA 02052

Phone: (508) 359-3825
Fax (508) 359-3356
william.pignato.b@bayer.com

Date Summary Prepared: March 2, 2001

2. **Device Information**

Proprietary Name:	Bayer Diagnostics ADVIA Centaur Toxoplasma IgM
Common Name:	Immunoassay, Toxoplasma Gondii
Device Classification:	Class II 21 CFR 866. 3780

3. **Predicate Device Information**

Name:	Vidas TOXO IgM K923166
Manufacturer:	bioMerieux

4. **Device Description**

Toxoplasma gondii is an intracellular parasitic protozoan that affects birds and mammals, with cats being the primary host. Infection is typically spread by eating raw or undercooked meat containing cysts or by coming in contact with oocyst-infected cat feces. Climate, dietary customs, and presence of cats influence the prevalence of *T. gondii* which can vary considerably by geographical location and age. In healthy immunocompetent individuals, infections are usually asyptomatic or subclinical. If toxoplasmosis is diagnosed during the early stages of infection, the disease can be treated effectively with antibiotic therapy.

In pregnant women, *T. gondii* infection poses a potential threat to the fetus. The risk of a pregnant woman passing infection to the fetus is approximately 25% in the first trimester and increases to approximately 65% in the third trimester. The earlier in the pregnancy that the mother is infected the greater the potential severity of congenital toxoplasmosis. If the fetus becomes infected, the infant may have symptoms such as lymphadenopathy, chorioretinitis, microcephaly and cerebral calcifications.

In immunosuppressed populations, such as cancer patients undergoing chemotherapy, transplants recipients, and AIDS patients, *T. gondii* has emerged as an important opportunistic pathogen leading to severe or fatal infections. The immunosuppressed state of these patients is thought to allow reactivation of a latent infection, and these patients may present symptoms such as headaches, confusion, fever, and focal neurological deficits.

Because isolation of the organism is difficult, toxoplasma IgM assays have been used in conjunction with clinical information in the diagnosis of *T. gondii* infection. In toxoplasma infected patients, the IgM antibody against *T. gondii* increases during acute infection but may be present for many months. A confirmed positive IgM anti-*T. gondii* test result is presumptive of a current or recent infection. In reactivated infections in immunosuppressed individuals, an IgM immunoresponse has not been demonstrated. The presence of IgG antibodies against *T. gondii* indicates that the individual has had a past infection, but the level of reactivity does not indicate how recently the infection occurred.

5. Statement of Intended Use

The ADVIA Centaur Toxoplasma IgM assay is an IgM antibody capture microparticle direct chemiluminometric *in vitro* diagnostic immunoassay for the qualitative detection of IgM antibodies to *Toxoplasma gondii* in serum or plasma (EDTA, heparin)

The ADVIA Centaur Toxoplasma M assay is used to measure IgM antibody against *T. gondii* which is presumptive of an acute, recent, or reactivated toxoplasma infection. Any measurement of IgM antibody to *T. gondii* must be performed in conjunction with the determination of IgG antibody to *T. gondii.*

6. Summary of Technological Characteristics

The ADVIA Centaur Toxoplasma M assay is an immunoglobulin class-capture sandwich immunoassay using direct, chemiluminometric technology. The anti-human IgM_{μ} monoclonal antibody is covalently coupled to paramagnetic particles in the Solid Phase. In the Lite Reagent, the *T. gondii* antigen is complexed with an anti-p30 monoclonal labeled with acridinium ester. Antibody-antigen complexes will form if toxoplasma IgM is present in the sample.

A direct relationship exists between the amount of toxoplasma IgM activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of positive or negative is determined using an Index Value. Refer to *Interpretation of Results* for a description of the Index Value.

7. Performance Characteristics

Expected Values

The incidence of toxoplasmosis varies considerably by the geographic location and age of patient. The following have been reported in the literature:

Location	Seroprevalance Rate
Europe	
France, Italy	50–85%, by region
Germany	20–72%, by region
United Kingdom	20%
Japan	24%
Africa	20–65%, by country

S. America	36–82%, by country
N. America	8–38%, by region

In this study, the toxoplasma IgM seropositive rate for samples obtained in the U.S. from asymptomatic pregnant women, hospital patients, blood donors, and HIV positive patients was determined to be 1.2%.

The distribution of ADVIA Centaur Toxoplasma M seropositive rates observed in this study are summarized below:

Population	N	Positive
Pregnant women	445	7 (1.6%)
Hospital patients	465	9 (1.9%)
Blood donors	540	4 (0.7%)
HIV positive patients	100	0 (0.0%)
Total	1550	20 (1.2%)

As with all in vitro diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.

Sensitivity and Specificity

Relative Agreement

The performance of the ADVIA Centaur Toxoplasma M assay was determined by testing a total of 1800 samples at three U.S. sites. The ADVIA Centaur results were compared to test results generated on a commercially available, automated toxoplasma IgM EIA. Fresh and frozen samples were used. Samples were obtained from the mid-Atlantic and Midwest regions of the United States as well as Germany and included the following populations: prenatal (N = 445), asymptomatic blood donors (N = 540), asymptomatic hospital patients (N = 465), and patients with confirmed toxoplasma IgM positive status. Of the 1800 specimens tested, 2 were equivocal by the ADVIA Centaur Toxoplasma M assay. Discordant results were found on 15 specimens. Further testing was done on the discordant samples using other commercially available tests for Toxoplasma IgM.

Relative Sensitivity

Using the alternative method, 256 tested positive for toxoplasma IgM antibody. Of the specimens that tested positive, 0 were equivocal, 254 were positive, and 2 were negative using the ADVIA Centaur Toxoplasma M assay. The initial relative sensitivity was 99.2%

Relative Specificity

Using the alternative method, 1542 tested negative for toxplasma IgM antibody. Of the specimens that tested negative, 2 were equivocal, 13 were positive, and 1527 were negative using the ADVIA Centaur Toxoplasma M assay. The initial relative specificity was 99.0%.

NOTE: Samples giving equivocal results were not included in the calculation of relative sensitivity, relative specificity, and relative agreement.

Relative Sensitivity, Specificity, and Agreement Before Resolution of Discordant Samples

Site	N	Relative Sensitivity (%)	Relative Specificity (%)	Relative Agreement (%)
1	1086	99.4 (154/155)	99.6 (926/930)	~~99.5 (1080/1085)~~ 99.5 (1080/1086
2	350	98.0 (50/51)	99.3 (294/296)	~~99.1 (344/347)~~ 98.3 (344/350)
3	364	100.0 (50/50)	97.5 (307/314)	~~98.1 (357/364)~~ 98.1 (357/364)
Total	1800	99.2 (254/256)	99.2 (1527/1540)	~~99.2 (1781/1796)~~ 98.9 (1781/1800)

NOTE: *Relative* refers to a direct comparison of ADVIA Centaur Toxoplasma M results to that of a similar assay. No attempt has been made to correlate with disease presence or absence, and no judgement can be made regarding the predicate assay's accuracy to predict toxoplasma disease.

Predicate Toxo IgM

ADVIA Centaur Toxoplasma M	POS	EQU	NEG	Total
POS	254	1	13	268
EQU	0	0	2	2
NEG	2	1	1527	1530
Total	256	2	1542	1800

Relative Sensitivity = 99.2% (254/256) 95% Confidence Limits 97.21 - 99.91
Relative Specificity = 99.2% (1527/1540) 95% Confidence Limits 98.56 - 99.55
Relative Agreement = 99.3% (1781/1796) 95% Confidence Limits 98.63 - 95.5

Consensus Testing

Further analysis of the 15 specimens with discordant results was performed using another commercially available EIAt for toxoplasma IgM. Of the 13 specimens that were positive by Centaur and negative by predicate EIA, 2 were positive, 1 was equivocal, and 10 were negative by consensus analysis. Of the 2 specimens that were positive by Centaur and negative by predicate EIA, 1 was negative and 1 was positive by consensus analysis.

CDC Panel

A characterized toxoplasma serology panel obtained from the Centers for Disease Control (CDC) was tested. The testing was performed to provide additional information about the performance of the ADVIA Centaur Toxoplasma M assay with a masked characterized serum panel. The panel consisted of 32 true positives, 3 serial dilutions of true positives, and 65 true negatives. The ADVIA Centaur Toxoplasma M assay correctly identified the 32 true positives, identified 2 of the 3

serial dilutions as positive, and 63 of the 65 true negatives. The assay was found to be 100% sensitive and 99.7% specific.

Evaluation of Potential Interfering Disease States

Potentially cross-reactive or interference samples were evaluated using the ADVIA Centaur Toxoplasma M assay and a commercially available, automated toxoplasma IgM EIA. Populations evaluated in the study included HAMA, RF, ANA, AMA, CMV, EBV, HSV, VZV, rubeola, syphilis, multiple myeloma, and parvovirus B19. Of the 113 samples tested, 112 (99.1%) generated negative results in the predicate EIA. Using the ADVIA Centaur Toxoplasma M assay, relative specificity of 99.1% was achieved on the predicate EIA negative samples. No significant interference or cross-reactivity for
these disease states was indicated.

Precision

Reproducibility of the ADVIA Centaur Toxoplasma M assay was determined as described in NCCLS protocol EP5-T2.[14] An eight-member panel was assayed two times in two separate daily runs, over a period of 20 days (n = 80). The following results were obtained using one reagent lot and a stored calibration curve:

			Within-run		Total*	
Panel Member	**N**	**Index**	**SD**	**% CV**	**SD**	**% CV**
Negative Control	80	0.12	0.10	8.84	0.011	9.53
Positive Control	80	2.57	0.076	2.94	0.114	4.44
1	80	0.18	0.022	12.16	0.023	12.72
2	80	0.40	0.022	5.51	0.029	7.18
3	80	0.73	0.035	4.88	0.045	6.22
4	80	1.39	0.052	3.77	0.077	5.57
5	80	4.26	0.168	3.95	0.203	4.78
6	80	8.91	0.302	3.39	0.455	5.11

*Includes within-run and run-to-run.

System reproducibility was determined by testing a 7 member panel with 2 reagent lots including 5 instruments and 3 sites over multiple days. The panel was assayed 3 times in each of 25 runs. The following results were obtained:

			Within-run		Total**	
Panel Member	**N**	**Index**	**SD**	**% CV**	**SD**	**% CV**
Negative Control	165	0.11	0.02	NA*	0.02	NA*
Positive Control	165	2.13	0.07	3.31	0.09	4.01
1	165	0.10	0.00	2.19	0.00	2.90
2	165	1.11	0.07	6.51	0.08	6.96
3	165	1.65	0.05	2.99	0.07	4.15
4	165	2.81	0.17	6.14	0.19	6.89
5	165	3.74	0.12	3.12	0.15	3.92
6	150	5.67	0.19	3.30	0.22	3.81
7	163	8.28	0.26	3.16	0.35	4.21

* Not applicable.

** Includes within-run and run-to-run.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 2 0 2001

Barbara Preisel-Simmons, Ph.D.
Principal Scientist, Quality Assurance
Bayer Corporation
63 North Street
Medfield, MA 02052-1688

Re: 510(k) Number: K010755
Trade/Device Name: Bayer Diagnostics ADVIA Centaur Toxoplasma IgM
Regulation Number: 866.3780
Regulatory Class: II
Product Code: LGD
Dated: June 19, 2001
Received: June 21, 2001

Dear Dr. Preisel-Simmons:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K010755

Device Name: Bayer Diagnostics ADVIA Centaur Toxoplasma IgM Assay

Indications for Use:

The ADVIA Centaur Toxoplasma IgM assay is an IgM antibody capture microparticle direct chemiluminometric *in vitro* diagnostic immunoassay for the qualitative detection of IgM antibodies to *Toxoplasma gondii* in serum or plasma (EDTA, heparin) in individuals including women of childbearing age utilizing the ADVIA Centaur System.

The ADVIA Centaur Toxoplasma M assay is used to measure IgM antibody against *T. gondii* which is presumptive of an acute, recent, or reactivated toxoplasma infection. Any measurement of IgM antibody to *T. gondii* must be performed in conjunction with the determination of IgG antibody to *T. gondii*.

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010755

(PLEASE DO NOT WRITE BELOW THIS LINE--CONTINUE ON ANOTHER PAGE, IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use X OR Over-The-Counter Use _____
(Per 21 CFR 801.109) **(Optional Format 1-2-96)**